

Claims

What is claimed is:

- July 5/2* 1. A nucleic acid delivery vehicle having at least a tissue tropism for fibroblast-like or macrophage-like cells.
- 5 *Sub Q 1* 2. A nucleic acid delivery vehicle having at least partially reduced tissue tropism for liver cells.
- July 5/2* 3. The vehicle of claim 1, wherein said vehicle has at least in part been deprived of at least 10 a tissue tropism for liver cells.
- Sub Q 1* 4. The vehicle of any one of claims 1-3, wherein said tissue tropism is provided by at least a part of a virus capsid or a functional derivative and/or analogue thereof.
- 15 5. The vehicle of claim 4, wherein said capsid comprises proteins, or functional parts, derivatives and/or analogues thereof, from at least two different viruses.
6. The vehicle of claim 5, wherein at least one of said viruses is an adenovirus.
- Sub Q 30* 7. The vehicle of claim 5 or claim 6, wherein at least one of said viruses is an adenovirus of subgroup B.
- 25 8. A vehicle according to any one of claims 5-7, wherein at least one of said proteins comprises a tissue tropism determining part of a fiber protein derived from a subgroup B adenovirus.

9. A vehicle according to claim 7 or claim 8, wherein said subgroup B adenovirus is adenovirus 16.

10. A vehicle according to any one of claims 7 through 9, further comprising:

5 at least one protein derived from an adenovirus not belonging to subgroup B, or a functional part, derivative and/or analogue thereof.

11. The vehicle of claim 10, wherein a protein or a functional part, derivative and/or analogue thereof not derived from an adenovirus of subgroup B is derived from an adenovirus of
10 subgroup C.

Sub q3

12. A vehicle according to anyone of the claims 1-11 comprising nucleic acid derived from an adenovirus.

15 13. A vehicle according to anyone of the claims 1-12, comprising nucleic acid derived from at least two different adenoviruses.

14. A vehicle according to claim 12 or claim 13, wherein said nucleic acid at least encodes a fiber protein comprising at least a tissue tropism determining part of a subgroup B adenovirus
20 fiber protein, in particular of a serotype 11, 16, 35 and/or 51, preferably of adenovirus 16 or a functional derivative and/or analogue thereof.

15. A vehicle according anyone of claims 12-14, wherein said adenovirus nucleic acid is a modified nucleic acid such that the capacity of said adenovirus nucleic acid to replicate in a target cell has been reduced or disabled, preferably through a deletion of at least part of the E1-
25 region.

16. A vehicle according to anyone of the claims 12-15, wherein said adenovirus nucleic acid is a modified nucleic acid such that the capacity of a host immune system to mount an immune response against adenovirus proteins encoded by said adenovirus nucleic acid has been reduced or disabled, preferably through a deletion of E2A and/or at least part of the E4-region.
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17. A vehicle according to anyone of claims 1-16, comprising a minimal adenovirus vector or an Ad/AAV chimaeric vector.
18. A vehicle according to anyone of claims 1-17, further comprising at least one nucleic acid of interest.
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19. A vehicle according to anyone of claims 1-18, wherein said vehicle is a subgroup B adenovirus capsid comprising at least one nucleic acid of interest.
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20. The vehicle of claim 19, wherein said nucleic acid further comprises subgroup B adenovirus nucleic acid.
21. The vehicle of claim 20, wherein said subgroup B adenovirus nucleic acid has been deprived of the capacity to express E1-region encoded proteins.
- 20
- Sub Q4
22. The vehicle of any one of claims 19-21, wherein said subgroup B adenovirus is adenovirus 16.
23. A method for producing a vehicle according to any one of claims 1-22, comprising providing a cell with means for the assembly of said vehicle wherein said means includes a means for the production of an adenovirus fiber protein, wherein said fiber protein comprises at least a tissue tropism determining part of a subgroup B adenovirus, in particular a serotype 11, 16, 35 and/or 51 adenovirus fiber protein or a functional derivative and/or analogue thereof.

24. A cell for producing a vehicle according to any one of claims 1-22, said cell comprising:
means for the assembly of said vehicle wherein said means includes a means for the production of an adenovirus fiber protein, said fiber protein comprising at least a tissue tropism determining part of a subgroup B adenovirus fiber protein.
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25. A method of treating a disease in a subject, said disease treatable by transfer of a nucleic acid encoding a therapeutic proteinaceous molecule or RNA to fibroblast-like or macrophage like cells, said method comprising administering the vehicle of according to claim 10 1 in a pharmaceutically acceptable manner in a pharmaceutically effective amount.
26. The method according to claim 25 wherein the disease is rheumatoid arthritis.
27. A method of delivering nucleic acid to fibroblast-like or macrophage-like cells, said 15 method comprising introducing the vehicle of claim 1 to said fibroblast-like or macrophage-like cells.
28. Construct pBr/Ad.BamRΔFib, comprising adenovirus 5 sequences 21562-31094 and 32794-35938.
- 20
29. A construct comprising adenovirus 5 sequences 21562-31094 and 32794-35938, and an adenovirus 16 nucleic acid encoding at least part of a fiber protein of adenovirus 16.
30. A construct comprising:
adenovirus 5 sequences 21562-31094 and 32794-35938;
an adenovirus 16 nucleic acid encoding at least part of a fiber protein of adenovirus 16;
and
a unique PstI-site in the proximity of the adenovirus 5 right terminal repeat, in the non-adenovirus sequence backbone of said construct.

31. A construct comprising:
adenovirus 5 sequences 3534-31094 and 32794-35938; and
an adenovirus 16 nucleic acid encoding at least part of a fiber protein of adenovirus 16.
- 5 32. A construct comprising adenovirus 5 sequences 3534-22443, 24033-31094 and 32794-
35938, and
an adenovirus 16 nucleic acid encoding at least part of a fiber protein of adenovirus 16.
- 10 33. A fibroblast-like or macrophage-like cell produced by the process of claim 27.
- 15 34. A method for at least in part removing synovium from a joint in an individual, said
method comprising:
administering to said individual's joint a nucleic acid delivery vehicle comprising
nucleic acid encoding at least herpes simplex virus thymidine kinase or a functional
part, derivative and/or analogue thereof; and
administering to said individual ganciclovir or a derivative and/or analogue thereof.

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